wherein said system is programmable to retrieve and handle either (a) the samples from every one of the chemical wells of said at least one multiwell plate or (b) the samples from a subset of chemical wells within said at least one multiwell plate.

## REMARKS

Applicants have amended Claims 1, 22, and 24. The specific changes to the amended claims are shown on a separate set of pages attached hereto and entitled VERSION WITH MARKINGS TO SHOW CHANGES MADE, which follows the signature page of this Amendment. On this set of pages, the insertions are underlined while the ~~deletions are stricken through~~. Applicants respond below to rejections and objections raised by the Examiner in the Office Action of July 18, 2002.

### I. Objections

Examiner has objected to Claims 10-12 because of their dependence on cancelled Claim 8. Claims 10-12 have now been cancelled.

### II. Rejections under 35 U.S.C. § 103

Claims 1-3, 20-21, and 24 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kelso *et al.* (WO 93/12431), and Claims 6, 22, and 23 stand rejected under 103(a) as being unpatentable over Kelso *et al.* in view of Shuttleworth, Inc., "Flat Panel Display News," February 1996. Applicants respectfully traverse.

**Kelso *et al.***

Kelso *et al.* describe a device (hereinafter "the Kelso device") that dilutes biological samples obtained from patients and then conducts certain assays on the diluted samples. The Kelso device comprises specimens in test tubes 186 on racks 184 as depicted best in Kelso *et al.* FIGS. 33, 34, and 42, and at p. 54, ll. 24-29; p. 56, ll. 22-33; p. 61, ll. 13-34. Each test tube contains a biological specimen from a patient, e.g., blood, urine, etc. Kelso, *et al.* p. 44, ll. 1-10. Kelso *et al.* teach that specimens from test tubes 186 are drawn sequentially from each test tube as they are ordered on the rack 184. The rack containing the test tubes simply moves one step at a time to the left to allow the boom 270 to draw the next sample. Kelso *et al.*, p. 61, ll. 20-24. Further, the Kelso device removes specimens from ALL of the test tubes 186. Kelso *et al.* state:

> The delivery and dilution sequence as just described repeats for the second through the sixth source specimens, during which the test wells . . . in the second and subsequent test rows . . . are filled.

* * *

> For the seventh and remaining source specimens, the position of the first probe 175 is again reinitialized to convey source fluid from the seventh and subsequent test tubes 186 beginning at the seventh column of the first and subsequent test rows; that is, at well (R1, C7) for the seventh specimen; at well (R2, C7) for the eight [sic, eighth] specimen; at well (R3, C7) for the eighth [sic, ninth] specimen; and so on.

Kelso *et al.*, p. 61, l. 13, to p. 62, l. 8. Kelso *et al.* do not teach or suggest jumping to any particular samples, skipping over any samples, stopping before all the samples are drawn, or moving in any order except left to right (relative to the rack as viewed as in FIG. 33). Accordingly, Kelso *et al.* merely teach that all the desired samples are lined up and each is processed in turn, there is nothing programmable in the sequence or selection once the samples are in the test tubes 186 and the test tubes are on the rack 184.

Furthermore, Kelso *et al.* state that

> The racks 184 are conveyed, one at a time, from the supply mechanism 180, into and through the sample pipetting station 162. There, fluid from the test tubes 186 is transferred to a waiting test carrier 12. The racks 184 then move to the discharge mechanism 182."

Kelso *et al.*, p. 43, ll. 28-33. The test tubes 186, therefore, are not returned to their original location, i.e. the supply mechanism 180, but rather are disposed of once the sample therein is aspirated for dilution. Kelso *et al.* explicitly state that once a rack clears the pipetting station, it is sent to the discharge mechanism, whereby the contents of the test tubes are discharged. The test tubes and/or the racks are NOT returned to the supply mechanism.

After a sample is retreived as described above, Kelso *et al.* disclose a process by which a series of dilutions can be prepared starting with a biological sample. This process is described from p. 56, l. 10 to p. 63, l. 11. In particular, the progressive dilution operations are described starting at p. 60, line 1 to p. 62, l. 8. Although the preparation of such dilutions is in a sense "programmable," it is not programmable with respect to the retrieval of any multiwell plate from a library.

As indicated above, it is the test tube racks 184 of the Kelso device that are most analogous to the multiwell plates of the pending claims. In the Kelso device, the test tube rack 184 carries a plurality of test tubes 186. A first probe 275 draws a volume of sample from the test tube 186 and delivers it to a test well 18. See p. 56, l. 22 to p. 57, l. 10.

However, when subsequent dilutions are made, the sample is taken from test well 18, not from test tube 186 on rack 184. Kelso states that the second probe 277 then prepares "diluted samples of the source fluid by drawing upon the fluid present in one well 18 previously filled by the first probe 275, adding to it a predetermined amount of diluent, and then discharging the diluted sample into one or more additional test wells 18." Kelso *et al.*, p. 53, ll. 17-29; See also p. 59, l. 30 to p. 60, l. 25.

There is nothing "programmable" in the manner of drawing samples from the test tube 186 on the rack 184. If any portion of the operation of a Kelso device is "programmable," it is the subsequent dilutions which involve the test wells 18 which are not the same as the sample storage wells which were initially selected from the library. Accordingly, the Kelso device cannot draw samples from the rack 184 in a programmable way as Claims 1, 2, 3, 20, 21, and 24 require. Accordingly, Kelso *et al.* do not teach the option of retrieving only some of the samples from a multi-well plate or from a test tube rack.

Pending Claims 1-3, 20-21, and 24 cover devices or systems having the capacity to selectively retrieve chemicals from the multiwell plate selected from the library. In Claims 1, 2, 3, and 24, this appears in the limitation that the "system is programmable to retrieve and handle ... the samples from a subset of chemical wells within said at least one multiwell plate." In Claims 20 and 21, it is in the limitation that "said devices handle chemicals from less than all of the wells of said retrieved plates." Accordingly, in these claims covering the present invention, retrieval of chemicals from the wells of said multiwell plate is programmable, which is to say that some subset of all the chemicals can be retrieved.

In the claimed invention, the samples can be retrieved in a variety of orders and groupings, including by groups defined by the user. FIG. 10A of the present disclosure depicts one possible interface by which the user may select samples for an assay. Indeed, the user can choose to retrieve all of the samples, or can choose to retrieve a subset. For example, the invention can allow a user to retrieve and study a group of samples which are not necessarily located close to one another in the library, but nonetheless share a particular property in which the user is interested (such as "date," "source," "media," etc.). Further, Claims 1-3, 20-21, and 24 include a liquid handler that can remove liquid from less than all of the addressable chemical wells. That is, once a multiwell plate comprising the addressable chemical wells is retrieved and

delivered to the chemical handler, the chemical handler can retrieve chemicals from some, but not all, of the wells of the multiwell plate.

The Kelso device is incapable of such programming; the racks 184 are simply conveyed one at a time from the supply mechanism. The operator does not programmably choose which racks are to undergo the test. Further, once a rack is brought to the pipetting station, the contents of ALL of the test tubes in each rack are pipetted out and deposited in the wells of a carrier.

Finally, Claims 1, 2, and 3 recite that the transport path of the system allows a multiwell plate containing addressable chemical wells to be returned to the library once the desired chemicals have been selected an a portion drawn out. Accordingly, in some embodiments, the remaining chemicals in the plate can be used at a later time. In Kelso *et al.*, the test tubes are simply discarded after the specimen is drawn.

**Shuttleworth**

Next, the Examiner has rejected Claims 6, 22, and 23 by relying on Shuttleworth in conjunction with Kelso *et al.* Shuttleworth discloses a conveyor system useful for various transport and handling applications in the manufacture of semiconductors. Applicant notes that the Examiner is correct that Shuttleworth teaches a buffer that can dynamically accumulate cassettes or pods before feeding them to a vertical conveyor. However, applicant respectfully submits that semiconductor manufacture and high throughput chemical screening are not analogous arts and that Shuttleworth is not properly combinable with Kelso *et al.* to provide the basis for a § 103 rejection. Applicant respectfully submits that Shuttleworth is not directed to the field of applicant's endeavor and is not pertinent to the particular problems with which the present invention is concerned. Accordingly, Shuttleworth may not properly be relied upon. *See* M.P.E.P. 2141.01(a) (citing *In re Oetiker*, 977 F.2d 1443, 1446, 24 U.S.P.Q.2d 1443, 1445 (Fed. Cir. 1992)).

First, Shuttleworth is not directed to the field of applicant's endeavor. Shuttleworth relates to the manufacture of glass substrates for the semiconductor industry. The present invention relates to screening chemicals for biological activity to be used in the chemical and/or pharmaceutical industries.

Second, Shuttleworth is not pertinent to the particular problems with which the present invention is concerned. Specifically, Claims 6, 22, and 23 recite a chemical storage buffer. The problems solved by the chemical storage buffer in the present invention are generally related to

the retrieval of different chemicals from the chemical library, particularly where the library is large and a non-trivial amount of time is required to retrieve those chemicals from different locations within the library. The present disclosure states that one function of the buffer is to allow the system to "retriev[e] chemicals [sic, chemical] plates from the buffer in a manner that minimizes processing time at workstations downstream of the plate buffer, while minimizing retrieval time from the storage and retrieval module." p. 11, ll. 23-25. This advantage is unique to a system in which items to be processed are drawn from various locations in a library, particularly a large library. A high-throughput chemical screening system, as in the present invention, is one such system.

Shuttleworth describes an apparatus useful for cassette transportation in semiconductor manufacturing. There is no teaching that the cassettes are retrieved from any "library," as in the present invention, and there is no teaching in Shuttleworth of selectively retrieving cassettes to make the process faster (as might correspond to retrieving particular multi-well plates based on the chemicals they contain). Indeed, there is no suggestion that the cassettes used in Shuttleworth differ from one another in any way. Even if the substrates are not all the same, there is no suggestion that the substrates or cassettes which are used will undergo any selective retrieval or sorting procedures, particularly in connection with the buffer. Accordingly, there is no suggestion that the buffers described in Shuttleworth facilitate selective retrieval or sorting of different items. As reasons for using a buffer in the present invention are unrelated to the reasons for using a buffer as disclosed in Shuttleworth, Shuttleworth may not properly be used as a basis for a § 103 rejection.

Even if Shuttleworth is considered as a reference in conjunction with Kelso *et al.*, the prior art of record still fails to teach or suggest all the elements of the present invention. Specifically, there is no teaching of an "automated multi-well plate retriever [that] comprises an integral plate storage buffer" as recited in Claim 6, or of "a chemical storage buffer coupled to and moving with said moving automated chemical retriever for temporarily storing chemicals retrieved from said storage locations" as recited in Claims 22 and 23. As Examiner has indicated, Kelso *et al.* "fail to teach a chemical plate buffer comprising a rack wherein the plates are stacked therein." Although Shuttleworth discloses a "buffer," the buffer is not "integral" to or "coupled" to any retriever. A Shuttleworth buffer is merely a static storage point at some location in a conveyor system. As discussed above, the buffer in the present invention functions

in close proximity to the retriever thereby solving unique problems associated with selectively retrieving chemicals from various locations in a library. In preferred embodiments, the buffer allows the retriever unit to retrieve multiple plates from the library in a manner that minimizes retrieval time and minimizes processing time downstream from the retriever. A buffer as described in Shuttleworth would not be useful for that purpose.

None of the cited references, either alone or in combination, disclose, teach, or suggest the presently claimed invention. Since a number of the elements of the independent claims are not disclosed or suggested by the cited references, the references either alone or in combination do not anticipate nor render obvious the claimed invention. Therefore, Applicants respectfully request the Examiner to reconsider and withdraw the rejections. Claims 1-3, 6, and 20-24 are pending in the application. Applicant respectfully submits that all claims are now in condition for allowance.

## CONCLUSION

The applicant has endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims pursuant to Examiner's objections and rejections under § 103, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. In light of these amendments and remarks, reconsideration and withdrawal of the outstanding objections and rejections is respectfully requested.

Any claim amendments which are not specifically discussed in the above remarks are not made for patentability purposes, and it is respectfully submitted that the claims satisfy the statutory requirements for patentability without the entry of such amendments. These amendments have only been made to increase claim readability, to improve grammar, or to reduce the time and effort required of those in the art to clearly understand the scope of the claim language.

If the Examiner has any questions which may be answered by telephone, she is invited to call the undersigned directly.

Respectfully submitted,

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**

1. (FOUR TIMES AMENDED) A high throughput chemical screening system comprising:

a chemical library comprising storage locations for ~~at least approximately 3000~~ a plurality of multi-well plates, each of which comprises ~~at least approximately 96~~ individual chemical wells for containing samples;

a computer controlled chemical well retriever for programmable selection and retrieval of ~~a subset~~ at least one of said multiwell plates comprising selected ones of said chemical wells;

a transport path coupled to said chemical library for receiving said ~~subset of said~~ at least one multiwell ~~plates~~ plate from and returning said ~~subset of said~~ at least one multiwell ~~plates~~ plate to said chemical library; and

a plurality of automated liquid handling devices operatively coupled to said transport path, whereby said high throughput chemical screening system is configured to process at least approximately 25,000 chemical samples in a 24 hour period;

wherein said system is programmable to retrieve and handle either (a) the samples from every one of the chemical wells of ~~an entire~~ said at least one multiwell plate or (b) the samples from a subset of chemical wells within said at least one multiwell plate.

22. (ONCE AMENDED) A chemical storage apparatus containing chemical samples to be retrieved comprising:

a plurality of storage locations for chemicals;

~~an~~ a moving automated chemical retriever configured to retrieve chemicals from said storage locations;

a chemical storage buffer ~~on~~ coupled to and moving with said moving automated chemical retriever for temporarily storing chemicals retrieved from said storage locations.

24. (TWICE AMENDED) A high throughput chemical screening system comprising:

a chemical library comprising storage locations for at least approximately 1000 multi-well plates, ~~and~~ each of which comprises individual chemical wells for containing samples, such that said library comprises at least approximately 100,000 addressable chemical ~~storage locations each containing a different chemical~~ wells;

a computer controlled chemical well retriever for programmable selection and retrieval of at least one of said multiwell plates comprising selected ones of said chemical wells;

a transport path coupled to said chemical library; and

a plurality of automated liquid handling devices coupled to said transport path;

wherein said system is programmable to retrieve and handle either (a) the samples from every one of the chemical wells of ~~an entire~~ said at least one multiwell plate or (b) the samples from a subset of chemical wells within said at least one multiwell plate.

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